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13. ABSTRACT (Maximum 200 words)

We have integrated microfluidic structures with optoelectronic lasers in the same device. Very sensitive and ultra-small laser sensors could be connected to fluidic systems by using microfluidic multiplexing technology and replication molded microfluidic chips. The basis of our sensor is a two-dimensional photonic crystal laser with an unusual cavity geometry that permits the introduction of analyte into the highest optical field region.This photonic crystal laser sensor can measure parts per million changes in the refractive index in volumes of several femtoliters, and is the "home run" we were looking for. We have used our microfluidic systems to perform a large number of analytical tasks, such as cell sorting, protein synthesis and even polymerase chain reaction (PCR) amplification of DNA. The photonc crystal laser sensors were also tested in different solutions, and their performance was calibrated by using standard index matching fluids, showing a linear response of the lasing frequency with changes in the refractive index. The fluidic delivery system together with the nano-spectroscopy tools developed in this program led to the possibility of interrogating and testing of picoliter volumes of solution with femtoliter sensitivity on compact and robust micro-chips.

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Caltech Contract: Monolithic Integration of Microfluidics and Optoelectronics for Biological Analysis

II. Technical Summary

We have recently developed photonic crystal lasers that permit the introduction of analyte within the peak of the optical field of the lasing mode. We have explored the design compromises for developing such sensitive low-threshold spectroscopy sources, and have demonstrated the operation of photonic crystal lasers in different ambient organic solutions. We have shown that nanocavity lasers can be used to perform spectroscopic tests on sub-femtoliter volumes of analyte, and use these lasers for high-resolution spectroscopy with single-molecule sensitivity.

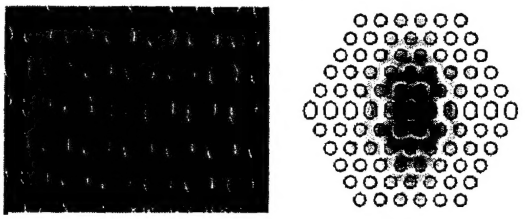

Figure 1. Scanning electron micrograph and calculated field distribution of a photonic nanocavity laser sensor

Until recently, the applications of planar photonic crystals have been restricted to large-scale integration of optical wavelength division multiplexing (WDM) components for telecommunications. Compact lasers, detectors, modulators, waveguides and prisms have been fabricated and demonstrated in semiconductor slabs of silicon, GaAs or InGaAsP [1]. These devices have been used to generate, concentrate and route light efficiently within nanophotonic chips. Discrete planar photonic crystal nanocavities with high quality factors and small mode volumes have also been applied to cavity QED experiments [2]. These take advantage of the strong overlap between a spectrally narrow light emitter placed into the intense electromagnetic fields of a high finesse optical nanocavity. Here, we propose another application of planar photonic crystal cavities in the development of chemical sensors, with high spectral resolution and excellent sensitivity to changes in the absorption or refractive index of their surrounding. By combining an unconventional cavity geometry (Figure 1) with optical gain at 1550nm, we have defined ultra-small sensor elements which can emit a very narrow spectrum. Since these are lithographically defined, such sources can easily be integrated into large arrays to perform biological and chemical analysis on extremely small reagent volumes with outstanding sensitivity.

To demonstrate this, photonic crystal nanolasers were fabricated from InGaAsP quantum well material. Optical gain was provided by four 9nm thick, compressively strained quantum wells, placed in the center of a 330nm thick InGaAsP slab. The emission from the quantum wells was in the range of $1300nm<\lambda<1600nm$, and these were embedded within a free standing membrane, patterned with a photonic crystal lattice as shown in Figure 1. The precise emission wavelength could be controlled either by scaling the lattice parameter, or by changing the size of the defect hole introduced into the lattice to form the cavity. The structures were tested using micro-photoluminescence approach, and were optically pumped at room temperature with 30ns pulses of 3μs periodicity (λ_{pump}=830nm). Further details of fabrication procedure and experimental method can be found in Reference 8.

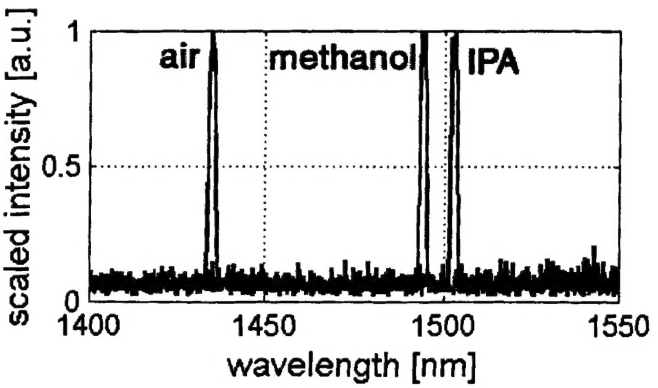

Figure 2. Measured laser spectra of photonic nanolaser sensor when filled with air, methanol

II. Chemical Sensing

We have already demonstrated that low-threshold laser cavities can be applied as chemical sensors. Our porous cavity design permits the introduction of analyte directly into the high optical field of the laser cavity. When the overlap between that introduced analyte and the optical field generated in the laser cavity is optimized, the sensitivity of a fabricated nanocavity sensor can be maximized. Moreover, the ultrasmall mode volume of our lasers permits the sensitivity to optical changes within sub-femtoliter volumes. Photonic crystal nano-cavities can support high optical fields with very small mode volumes (V_{mode}), and such structures are expected to be ideal for the analysis of reagent volumes below 10^{-18} liters. This will enable the sensing and analysis of individual organic molecules or self-assembled quantum dots, and offers a unique opportunity to achieve strong interaction between light and molecules on a nano-scale level. The introduction of absorbing or fluorescing molecules into such cavities is expected to have a large

influence on the optical signature, and in turn the high fields obtained can be used to excite nonlinear effects and can be used for spectroscopy on the cavity contents. We have shown that, when properly designed, room temperature lasers can operate within an analyte, and changes in refractive index of the material within the laser cavity can be optically detected (Figure 3).

The simplest method of optically sensing ambient material uses the laser spectrum to determine the cavity length and thus the refractive index of a reagent within the cavity. This method uses the wavelength shifts in the laser spectrum when the laser is immersed into a solution or exposed to a material to measure its refractive index. In this method, the sensitivity of the sensor depends on the smallest change in refractive index that can be optically detected. In passive devices, this is related to the width of the cavity resonance Fabry-Perot peak which in turn is determined by cavity quality Q, and can be as small as ~0.2nm in the presented cavity design. However, a laser linewidth can be much narrower than the Fabry-Perot cavity peak, and even smaller shifts in the lasing wavelength can be detected by taking advantage of the spectral narrowing from stimulated emission above laser threshold. To test the influence of a change in ambient refractive index on the laser spectrum of a cavity, we have backfilled our photonic crystal lasers with isopropyl alcohol and methanol. Figure 2 shows position of the resonances from six different lasers after immersion in air, isopropyl alcohol (IPA) and methanol. It can be seen that wavelength shifts of up to 67nm can be observed when a cavity is immersed in IPA. This red-shift corresponds to a change in refractive index from 1.0 to 1.377, and yields roughly 1nm spectral shift for a 0.0056 change in refractive index. When IPA is replaced with methanol (n=1.328), the laser resonance experiences a blue shift of ~9nm, which is again in good agreement with predicted shift of ~13nm from our theoretical predictions (Figure 2). We have also investigated the dependence of the cavity resonance wavelength on the lithographic laser geometry, particularly the lattice constant and the dislocation in the photonic crystal cavity.

Microfluidic Sample Delivery: There have been many driving forces to exploit the potential benefits of miniaturized apparatus relative to systems of conventional size, including reduced consumption of samples and reagents, shorter analysis times, greater sensitivity, portability that allows in-situ and real-time analysis, and disposability [4]. A unifying vision for the field has been the notion that, in the same way that integrated circuits use miniaturized transistors to automate computation (Fig. 3), microfluidic chips could accomplish large-scale automation of biological processing using nanoliter volumes. The past decade was a period of furious technological development, and many individual microfluidic components with the ability to perform biological manipulations on nanoliter volumes were demonstrated in the Caltech bioflips program.

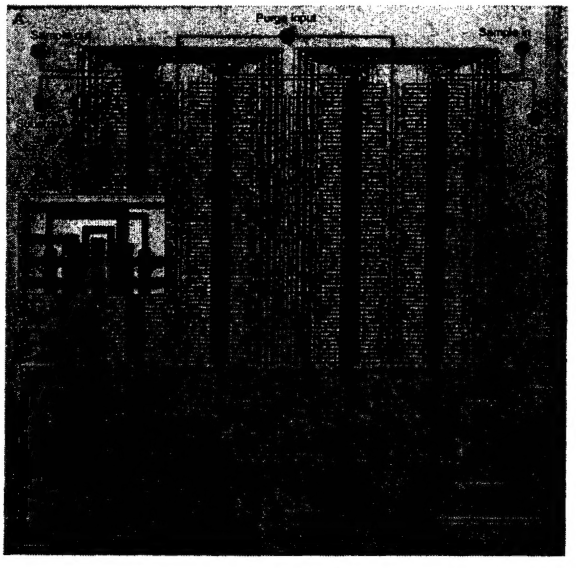

Fig. 3. Optical micrograph of a microfluidic assay chip

Individual microfluidic components, even if they are capable of analyzing nanoliters of material, are often of little use unless they can be integrated together in a functional system. An exception to this rule is when a microfluidic component takes advantage of novel fluid physics only available at the microscale. There have been several scientific demonstrations that take advantage of these effects and some of them find their way to commercialization. Today, we are seeing the emergence of truly integrated microfluidic systems for biotechnology that operate on nanoliters of material, which can be termed "microfluidic systems". The main technology platforms for microfluidic research are based on microfabrication techniques, such as photolithography, that were originally developed for the semiconductor industry. The initial motivation was the idea that fabrication technologies used for manipulating electrons in ever more complicated ways could also be used to make devices that would manipulated fluids. Common substrates used in these devices are glass and silicon, but such hard materials are not ideally suited for implementing robust liquid control systems such as valves and pumps. Thus, alternative fabrication methods and materials such as soft lithography with silicone rubber became popular, resulting in the emergence of a wide variety of techniques and materials to make fluidic devices. Nevertheless, there are many interesting analogies between integrated microfluidic system design and the development of integrated circuits, and it remains instructive to make conceptual comparisons between the two fields.